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# Set-membership identifiability and guaranteed parameter estimation for nonlinear uncertain dynamical systems

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**Abstract:** Definitions of identifiability and methods for checking this property for linear and nonlinear systems are now well established. Recently, some works (Jauberthie et al. [2011], Braems et al. [2001]) have provided identifiability definitions for set-membership models in a bounded-error context and established links with classical identifiability definitions. These works are summarized in the first part of the paper, recalling the two complementary definitions : *set-membership identifiability* that is conceptual and  *$\mu$ -set-membership identifiability* that can be put in correspondence with existing set-membership parameter estimation methods (Jauberthie et al. [2011]). In the second part, two methods for checking set-membership identifiability and  $\mu$ -set-membership identifiability are proposed. The first one is an extension of a method proposed by Pohjanpalo [1978] based on the power series expansion of the solution that accounts for the initial conditions of the system. It generalizes to non-linear systems the initial extension provided in (Jauberthie et al. [2011]). The second method is based on differential algebra and makes use of relations linking the observations, the inputs and the unknown parameters of the system. Classically, when using this method, initial conditions are not considered but it has been shown recently (Saccomani et al. [2004]) that they can change the identifiability results. In this paper, an extension using initial conditions is proposed. In the third part of the paper, a numerical parameter estimation method is deduced from the differential algebra method and an example is presented.

*Keywords:* Identifiability; Uncertain dynamic systems; Nonlinear models; Bounded disturbances; Parameters estimation

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## 1. INTRODUCTION

In most models, some parameters characterizing the internal behavior of the represented system are not directly accessible to measure. This is for example the case for biological and physiological systems. These parameters are usually estimated through an iterative learning algorithm. However, before searching for their values, it is essential to study the model structure identifiability to assess whether the set of unknown parameters can be uniquely determined from the data assumed to be generated by a model with the same structure. Indeed, if a model is not identifiable, the numerical search procedures can fail. In that case, some supplementary data have to be provided, or the parameters admissibility domain has to be reduced.

In the literature, different approaches have been proposed for studying the global identifiability of nonlinear systems. We can mention for example, the Taylor Series approach of Pohjanpalo [1978]. He proposed a method based on the analysis of a power series expansion of the output which gives rise to an algebraic system constituted of an infinite number of equations. A second method is based on the local state isomorphism theorem (Walter and Lecourtier [1982], Chappell and Godfrey [1992], Denis-Vidal et al. [2001], Chapman et al. [2003]). It leads to study the solution of a specific set of partial differential equations.

A third one is a method based on differential algebra that was

introduced in Diop and Fliess [1991], M. Fliess [1993], Ljung and Glad [1994] and Ollivier [1997]. It allows one to obtain relations linking the observations, the inputs and the unknown parameters of the system. In the first works, the initial conditions were ignored. However, without any assumptions on the model, the identifiability of the model without any consideration on initial conditions does not imply the identifiability of the model with initial conditions (Audoly et al. [2001]). A few developments were proposed to consider the initial conditions (Saccomani et al. [2004], Denis-Vidal et al. [2001], Verdière et al. [2005]). In the latter paper, some numerical algorithms were developed, built on the identifiability study, to give a first estimation of the parameters without any a priori knowledge about them.

When modeling a system, several sources of uncertainty exist due, for example, to the inaccuracies in the measurements. For analyzing uncertain models, new identifiability definitions applying to set-membership (SM) models in a bounded error context have been proposed in (Jauberthie et al. [2011]) and (Braems et al. [2001]). The pioneering paper by Braems et al. [2001] outlines that interval based methods and interval constraint propagation can be used to test for a new definition of global identifiability. In contrast to structural global identifiability, the new property no longer allows for the existence of atypical regions in the domain of interest. This is actually a

byproduct of using interval methods for testing for it. But, what is really an interpretation of identifiability in the SM context is only presented as a practical condition. Indeed, instead of imposing parameters corresponding to a given input-output trajectory to be strictly different, they are allowed to be distant by a given  $\varepsilon$ , which provides a stopping condition to the numerical test. It is only recently that Jauberthie et al. [2011] formalized the above property and numerical test as a whole by introducing two complementary definitions for the identifiability of error-bounded uncertain models, namely *set-membership identifiability* (SM identifiability) and  $\mu$ -*set-membership identifiability* ( $\mu$ -SM identifiability). The first one is conceptual whereas the second one can be put in correspondence with interval based methods and the specified precision threshold  $\varepsilon$ .

In this paper, two methods for checking SM identifiability and  $\mu$ -SM identifiability are proposed. They contrast the numerical method of Braems et al. [2001] which is limited to linear models and models whose analytical solution is known. The first method is an extension of a method proposed by Pohjanpalo [1978] based on the power series expansion of the solution that accounts for the initial conditions of the system. It generalizes to non-linear systems the extension already provided in Jauberthie et al. [2011]. The second method is based on differential algebra and makes use of relations linking the observations, the inputs and the unknown parameters of the system. In the presented work, an extension using initial conditions is proposed.

In the last part of the paper, a numerical parameter estimation method is built on top of the differential algebra method. The relations mentioned above are used to estimate the uncertain parameters of the model in an analytical way. Linking identifiability analysis and parameter estimation, we can guarantee when the solution set for the system (1) reduces to one connected set. An example in pharmacokinetic is presented.

The paper is organized as follows. Section 2 presents the considered model and section 3 the definitions of identifiability in a bounded error context. In section 4, the two methods for analysing SM identifiability are developed. The numerical method to estimate the parameters building on the differential algebra method is then presented in section 5 and illustrated by an example. Section 6 concludes the paper and envisions several perspectives.

## 2. PROBLEM FORMULATION

The problem considered in this paper is the identification relying on identifiability assessment of bounded uncertain parameter systems (controlled or uncontrolled) represented by SM models of the following form:

$$\Gamma_1^P = \begin{cases} \dot{x}(t, p) = f(x(t, p), u(t), p), \\ y(t, p) = h(x(t, p), p), \\ x(t_0, p) = x_0 \in X_0, \\ p \in P \subset \mathcal{U}_P, \\ t_0 \leq t \leq T, \end{cases} \quad (1)$$

where  $x(t, p) \in \mathbb{R}^n$  and  $y(t, p) \in \mathbb{R}^m$  denote the state variables and the outputs at time  $t$  respectively,  $u(t) \in \mathbb{R}^r$  is the input vector at time  $t$ . The initial conditions  $x_0$ , are supposed to belong to a bounded set  $X_0$ . The functions  $f$  and  $h$  are real and analytic on  $M$ , where  $M$  is an open set of  $\mathbb{R}^n$  such that  $x(t, p) \in M$  for every  $t \in [t_0, T]$  and  $p \in P$ .  $T$  is a finite or infinite time bound. The vector of parameters  $p$  belongs to a connected set of parameters  $P$ .  $P$  is supposed to be a subset of

$\mathcal{U}_P$  where  $\mathcal{U}_P$  is an a priori known set of admissible parameters.  $\mathcal{U}_P$  is either included in  $\mathbb{R}^P$  or equal to  $\mathbb{R}^P$ . In the case of uncontrolled models,  $u$  is equal to 0.

## 3. SET-MEMBERSHIP IDENTIFIABILITY

This section proposes a formulation of the SM identifiability problem for the class of systems described in section 2 and formalized by (1).

### 3.1 Definitions

Two definitions of global SM identifiability are provided, as well as their local counterpart. The first one is a conceptual definition, whereas the second one, relying on the definition of a measure  $\mu$ , can be put in correspondence with operational SM estimation methods.

In these definitions,  $Y(P, u)$  (respectively  $Y(P)$ ) denotes the set of outputs, solution of  $\Gamma_1^P$  with the input  $u$  (resp. when  $u = 0$ ). In the case of controlled systems (the case of uncontrolled systems is considered subsequently), the following definitions are given:

*Definition 3.1.* The model  $\Gamma_1^P$  given by (1) is globally SM identifiable for  $P^* \neq \emptyset$ ,  $P^* \subset \mathcal{U}_P$  if there exists an input  $u$  such that  $Y(P^*, u) \neq \emptyset$  and  $Y(P^*, u) \cap Y(\bar{P}, u) \neq \emptyset$ ,  $\bar{P} \subset \mathcal{U}_P \implies P^* \cap \bar{P} \neq \emptyset$ .

Let us now consider a bounded set  $\Pi$  of  $\mathbb{R}^P$  and let us note  $\mu(\Pi)$  the *diameter* of  $\Pi$ .  $\mu(\Pi)$  is given by the least upper bound of  $\{d(\pi_1, \pi_2), \pi_1, \pi_2 \in \Pi\}$  and  $d$  is a classical metric on  $\mathbb{R}^P$  (Bourbaki [1989]). If  $\Pi$  is not bounded, we define  $\mu(\Pi) = +\infty$ .

In the following definition, the set  $P^*$  is supposed bounded and  $\mu(P^*)$  is said *as small as desired* when it may be taken as tending to zero.

*Definition 3.2.* The model  $\Gamma_1^P$  given by (1) is globally  $\mu$ -SM identifiable for  $P^* \neq \emptyset$  with  $\mu(P^*)$  as small as desired, if there exists an input  $u$  such that  $Y(P^*, u) \neq \emptyset$  and  $Y(P^*, u) \cap Y(\bar{P}, u) \neq \emptyset$ ,  $\bar{P} \subset \mathcal{U}_P \implies P^* \cap \bar{P} \neq \emptyset$ .

The above definition differs from definition 3.1 in the sense that the set  $P^*$  may be taken as small as desired, i.e.  $\mu(P^*)$  may tend to zero. If the diameter of  $P^*$  remains higher than or equal to a threshold  $\varepsilon$ , i.e.  $\mu(P^*) \geq \varepsilon$ , then we refer to  $\varepsilon$ -SM *identifiability*. This definition will be shown to have practical importance in section 3.3.

To account for possible singularities in  $\mathcal{U}_P$ ,  $\mu$ -SM identifiability can be generically extended into *structural  $\mu$ -SM identifiability*, which means that the model  $\Gamma_1^P$  is  $\mu$ -SM identifiable for all  $P \subset \mathcal{U}_P$  except for a subset of points of zero measure in  $\mathcal{U}_P$ . Let us notice that defining the structural counterpart of SM identifiability, as given by definition 3.2, is not relevant given that in definition 3.1  $P^*$  cannot be of zero measure.

*Proposition 3.1.* Global  $\mu$ -SM identifiability for  $P^*$  implies global SM identifiability for  $P^*$  but the inverse is not true.

*Proof* – The implication is obvious. The fact that the inverse implication is not true is proved with a counter-example. Let us consider the following uncertain model in which  $\omega$  is an unknown parameter belonging to an initial interval:

$$\begin{cases} \dot{x}_1 = x_1 + t \cos(\omega), \\ x_1(0) = \cos\left(\frac{\pi\theta}{50}\right) \text{ with } \theta \in [0, 75]. \end{cases}$$

Its solution is  $x_1(t) = \cos(\pi\theta/50)e^t + (-1 - t + e^t)\cos(\omega)$ . An admissible set for  $\omega$  is taken as  $\mathcal{U}_{\mathcal{P}} = [0, 2\pi]$ . For  $\theta = 25$  or  $75$ , the solution is equal to  $x_1(t) = (-1 - t + e^t)\cos(\omega)$ . In this case, if  $\omega \in P^* = [\pi/2, 3\pi/2]$  then the model is globally SM identifiable but not  $\mu$ -SM identifiable. Indeed, for the global SM identifiability, no trajectory arising from the systems whose parameters are in  $P^*$  is identical to a trajectory arising from the complementary of  $P^*$  in  $\mathcal{U}_{\mathcal{P}}$ . However, if the diameter of  $P^*$  is smaller, for the two disjoint subsets of  $P^*$ ,  $P_1^* = [\pi, 3\pi/2]$  and  $P_2^* = [\pi/2, 3\pi/4]$ , there exist common trajectories. Consequently,  $\mu(P^*)$  cannot be taken as small as desired.  $\square$

Local definitions of  $(\mu)$ -SM identifiability can be given by considering an open neighborhood  $W$  of  $P^*$  in which  $\Gamma_1^P$  is globally  $(\mu)$ -SM identifiable for  $P^*$  with  $\mathcal{U}_{\mathcal{P}}$  restricted to  $W$ .

If the model (1) is neither globally  $(\mu)$ -SM identifiable nor locally  $(\mu)$ -SM identifiable, it is said *non  $(\mu)$ -SM identifiable*.

### 3.2 Case of uncontrolled models

In the case of uncontrolled systems, the following definitions can be given.

*Definition 3.3.* The model  $\Gamma_1^P$  given by (1) is globally SM identifiable for  $P^* \neq \emptyset$ ,  $P^* \subset \mathcal{U}_{\mathcal{P}}$  if  $Y(P^*) \neq \emptyset$  and  $Y(P^*) \cap Y(\bar{P}) \neq \emptyset$ ,  $\bar{P} \subset \mathcal{U}_{\mathcal{P}} \implies P^* \cap \bar{P} \neq \emptyset$ .

*Definition 3.4.* The model  $\Gamma_1^P$  given by (1) is globally  $\mu$ -SM identifiable for  $P^* \neq \emptyset$ ,  $P^* \subset \mathcal{U}_{\mathcal{P}}$ ,  $\mu(P^*)$  as small as desired, if  $Y(P^*) \neq \emptyset$  and  $Y(P^*) \cap Y(\bar{P}) \neq \emptyset$ ,  $\bar{P} \subset \mathcal{U}_{\mathcal{P}} \implies P^* \cap \bar{P} \neq \emptyset$ .

As previously, local definitions can also be given.

### 3.3 Correspondence with operational interval based parameter estimation

This section first provides some concepts related to the manipulation of sets, then discusses interval based set inversion, exemplified by the algorithm SIVIA (Set Inversion Via Interval Analysis), as a framework in which the parameter estimation problem can be casted (Jaulin and Walter [1993]). An interpretation of  $\varepsilon$ -SM identifiability is then exhibited and shown to be a formalization of the interval based test proposed in Braems et al. [2001] in the framework of Interval Constraint Propagation (ICP).  $\varepsilon$ -SM identifiability is indeed shown to generalize classical identifiability to sets whose dimension can be controlled.

When manipulating sets of values, it is important to be able to check whether one set is included in another set or not. Given two subsets  $S_1$  and  $S_2$  of  $\mathbb{R}^n$ , one wants to test whether  $S_1$  is included in  $S_2$  or not. This test, known as the *inclusion* test is used to prove that all points in a given set satisfy a given property or to prove that none of them does.

Conversely, if two sets intersect, their intersection inherits the properties of the two sets. It is hence often desirable to reduce a set to its intersection with respect to another set, which is obtained through *contraction*. The *contraction* of  $S_1$  with respect to  $S_2$  is a smaller set  $s$  such that  $S_1 \cap S_2 = s \cap S_2$ . If  $S_2$  is the feasibility set of a problem and  $s$  turns out to be empty, then the set  $S_1$  does not contain the solution.

Interval analysis makes use of specific sets, also known as *boxes*. A real interval is a closed and connected subset of

$\mathbb{R}$  denoted  $[\underline{x}, \bar{x}] = \{x \in \mathbb{R}, |\underline{x} \leq x \leq \bar{x}\}$ . A box  $[x]$  is an interval vector  $[\underline{x}, \bar{x}]$ , that is a vector with interval components<sup>1</sup>. In SIVIA, inclusion and contraction are used to test if a box can or cannot be removed from the solution set. When no conclusion can be drawn, the box is bisected and each of the sub-boxes can be tested in turn (this corresponds to a *branch-and-bound* algorithm). The same principles are used in ICP.

Consider the problem of determining the solution set for the unknown quantities  $p$  defined by

$$S = \{p \in \mathcal{U}_{\mathcal{P}} \mid \Phi(p) \in [y]\} = \Phi^{-1}([y]) \cap \mathcal{U}_{\mathcal{P}}, \quad (2)$$

where  $[y]$  is known a priori,  $\mathcal{U}_{\mathcal{P}}$  is an a priori search set for  $p$  and  $\Phi$  a nonlinear function not necessarily invertible in the classical sense. (2) involves computing the reciprocal image of  $\Phi$ . This can be solved using the algorithm SIVIA, which recursively explores all the search space without losing any solution. SIVIA delivers a guaranteed enclosure of the solution set  $P$  such as  $\underline{P} \subseteq P \subseteq \bar{P}$ .

The inner enclosure  $\underline{P}$  is composed of the boxes that have been proved feasible. To prove that a box  $[p]$  is feasible it is sufficient to prove that  $\Phi([p]) \subseteq [y]$ . Conversely, if it can be proved that  $\Phi([p]) \cap [y] = \emptyset$ , then the box  $[p]$  is unfeasible. Otherwise, no conclusion can be reached and the box  $[p]$  is said undetermined. The latter is then bisected in two sub-boxes that are tested until their size reaches a user-specified precision threshold  $\varepsilon > 0$ . Such a termination criterion ensures that SIVIA terminates after a finite number of iterations.

SM identifiability does not provide the means to control the set  $P^*$  that is tested for identifiability. This points out the practical interest of  $\mu$ -SM identifiability which is defined through a measure  $\mu(\cdot)$ . The measure  $\mu(\cdot)$  allows one to control the diameter of  $P^*$ . In particular,  $\varepsilon$ -SM identifiability is defined for the diameter of  $P^*$  higher or equal to  $\varepsilon$ , i.e.  $\mu(P^*) \geq \varepsilon$ . The diameter of  $P^*$  can hence be put in correspondance with the user-specified precision threshold of SIVIA. Consequently,  $\varepsilon$ -SM identifiability provides the means to guarantee that the estimate provided by SIVIA when the precision threshold is taken equal to  $\varepsilon$  consists of a connected set.

$\varepsilon$ -SM identifiability is actually a formalization of the ICP numerical test proposed by Braems et al. [2001] to check global identifiability in a domain. Instead of imposing parameters corresponding to a given input-output trajectory to be strictly different, they allow them to be distant by a given  $\varepsilon$ , which provides a stopping condition to the ICP numerical method.

Ultimately,  $\mu$ -SM identifiability subsumes classical identifiability and SM identifiability as defined in definition 3.1 as it provides the mean to control the set  $P^*$ . This is possible thanks to the measure  $\mu(\cdot)$ . When  $\mu(P^*)$  tends to 0,  $\mu$ -SM identifiability comes back to classical identifiability. When  $\mu(P^*)$  is kept higher or equal to  $\varepsilon$ , it results in  $\varepsilon$ -SM identifiability.  $\varepsilon$  is not necessarily small, so the control of the dimension of the set  $P^*$ .

## 4. ANALYSIS OF SM IDENTIFIABILITY

Two methods are proposed in this paper for analysing  $(\mu)$ -SM identifiability: the first one is based on the power series expansion of the solution and the second one on differential algebra. For these two methods, the notion of partial injectivity

<sup>1</sup> Obviously, a box  $[x]$  of dimension  $n$  is a subset  $X$  of  $\mathbb{R}^n$ . In the following, the two notations are used equally.

using interval analysis is needed and is recalled in the first subsection.

#### 4.1 Partial injectivity

First of all, remember the definition of partial injectivity of a function given in Lagrange et al. [2007].

*Definition 4.1.* Consider a function  $f : \mathcal{A} \rightarrow \mathcal{B}$  and any set  $\mathcal{A}_1 \subseteq \mathcal{A}$ . The function  $f$  is said to be a partial injection of  $\mathcal{A}_1$  over  $\mathcal{A}$ , noted  $(\mathcal{A}_1, \mathcal{A})$ -injective, if  $\forall a_1 \in \mathcal{A}_1, \forall a \in \mathcal{A}$ ,

$$a_1 \neq a \Rightarrow f(a_1) \neq f(a).$$

$f$  is said to be  $\mathcal{A}$ -injective if it is  $(\mathcal{A}, \mathcal{A})$ -injective.

In Lagrange et al. [2007], an algorithm based on interval analysis for testing the injectivity of a given differentiable function is presented and a solver called ITVIA (Injectivity Test Via Interval Analysis) implemented in C++ is mentioned.

#### 4.2 Power Series Expansion Method (PSE Method)

The PSEM method is inspired of Pohjanpalo [1978], which studies identifiability in using the Taylor series expansion of the solution.

Consider  $P^*$  a connected set and  $Y(P^*, u)$  a set of model outputs,  $a_0(\cdot) \in Y(P^*, u)$  (resp.  $a_k(\cdot)$ ) a particular output (resp. the  $k$ th time derivative of  $a_0(\cdot)$ ). Then, consider the following assumptions which are referred to as  $H$  in the following:

- Denote the set of feasible states by  $S$ ,
- Let  $u(\cdot)$  and  $x(0)$  be such that  $x(t) \in S$  for all  $t \in [0, T]$
- For all possible trajectories  $x(\cdot)$ , the function  $f(x(\cdot), u(\cdot), p)$  admits a Taylor series expansion on  $[0, T]$  or the function  $f(x, u(\cdot), p)$  is lipschitzian on  $[0, T]$  for all states  $x \in S$ .

The following theorem gives a necessary condition for having global  $(\mu)$ -SM identifiability. It can be used for proving non  $(\mu)$ -SM identifiability for controlled models.

*Theorem 1.* Under the assumptions  $H$ , if  $\Gamma_1^P$  is globally SM identifiable (resp. globally  $\mu$ -SM identifiable) for  $P^* \neq \emptyset$  for an input  $u$  and  $a_0(\cdot) \in Y(P^*, u)$ , then the system:

$$\frac{d^k}{dt^k}[h(x(0, p), p)] = a_k(0), \quad k = 0, 1, \dots, +\infty, \quad (3)$$

where  $h$  is the observation function of system (1) admits at least one solution in the connected set  $P^*$  (resp. a unique solution).

*Proof* – By assumption,  $h$  is analytic and (3) admits solutions in  $P^*$ .

If  $\Gamma_1^P$  is globally  $\mu$ -SM identifiable, there is a one-to-one correspondence between a trajectory and a parameter vector thus the unicity of the solution.  $\square$

The following theorem gives a sufficient condition for proving that  $\Gamma_1^P$  is globally SM identifiable for  $P^*$ .

*Theorem 2.* If there exists  $u$  such that  $Y(P^*, u) \neq \emptyset$  and for all  $a_0(\cdot) \in Y(P^*, u)$ , the solutions of (3) are in  $P^* \neq \emptyset$  then  $\Gamma_1^P$  is globally SM identifiable for  $P^*$  for this input  $u$ .

*Proof* – Suppose that  $Y(P^*, u) \cap Y(\bar{P}, u) \neq \emptyset$  for  $\bar{P} \subset \mathcal{U}_p$ . Thus there exists a trajectory  $y^* \in Y(P^*, u) \cap Y(\bar{P}, u)$ . In particular, there exist  $p^* \in P^*, \bar{p} \in \bar{P}$  solutions of (3) for which the right member  $a_k(\cdot)$  corresponds to  $y^{*(k)}(\cdot)$ . Hence,  $\bar{p} \in P^*$  and  $P^* \cap \bar{P} \neq \emptyset$ .  $\square$

*Remark*– For uncontrolled systems, we have equivalent conditions to be satisfied autonomously.

An additional condition is required for the system  $\Gamma_1^P$  to be globally  $\mu$ -SM identifiable or  $\varepsilon$ -SM identifiable for  $P^*, \varepsilon > 0$ . Indeed, since  $P^*$  can be as small as possible, the parameter  $\bar{p}$  may not be included in  $P^*$ . However, an injectivity hypothesis allow one to obtain  $\mu$ -SM identifiability or  $\varepsilon$ -SM identifiability for  $P^*$  as it is seen in the following theorem.

*Theorem 3.* Suppose there exists  $u$  such that for any  $a_0(\cdot) \in Y(P^*, u)$ , the solutions of (3), for a finite number  $d$  of equations are in a connected set  $P^* \neq \emptyset$ . If the function  $\phi : p \in P^* \mapsto (h(x(0, p), p), \dots, \frac{d^{d-1}}{dt^{d-1}}[h(x(0, p), p)]) \in (\mathbb{R}^m)^d$  is  $(P^*, \mathbb{R}^p)$ -injective (resp. except on a subset of  $P^*$  whose diameter is less than  $\varepsilon$ ), then  $\Gamma_1^P$  is  $\mu$ -SM identifiable for  $P^*$  (resp.  $\varepsilon$ -SM identifiable for  $P^*$ ).

*Remark* –  $d - 1$  is the number of times that  $y(t, p) = h(x(t, p), p)$  must be derived for the resulting system taken at  $t = 0$  admits solutions.

*Proof* – The injectivity hypothesis assures that the trajectories evaluated with parameters in  $P^*$  are all distinct.  $\square$

For obtaining the system (3), complex math developments are generally required. However, some classes of systems have nice properties and are easily solved, for example linear systems (Pohjanpalo [1978]).

*Example 1:* Consider as  $\Gamma_1^P$  the following uncertain system taken from Vajda et al. [1989]:

$$\begin{cases} \dot{x}_1 = -(k_{21} + k_{31})x_1 + u, & x_1(0) = x_{10}, \\ \dot{x}_2 = k_{21}x_1 - x_2, & x_2(0) = 0, \\ \dot{x}_3 = k_{31}x_1 - c_{13}x_3, & x_3(0) = x_{30}, \\ y = x_2 + c_{13}x_3, \end{cases} \quad (4)$$

where the unknown parameters are  $k_{21}, c_{13}, \mathcal{U}_p = \mathbb{R}^2$ . Suppose that  $x_{i0} \in [\underline{x}_{i0}, \bar{x}_{i0}]$ ,  $i = 1, 3$  and  $a_0(\cdot) \in Y_m$ . Suppose too that  $0 \notin [\underline{x}_{30}, \bar{x}_{30}]$ .

In this example, the set of parameters  $P^*$  containing  $(k_{21}, c_{13})$  is searched so that  $\Gamma_1^P$  is globally  $\mu$ -SM identifiable for  $P^*$ . For this, the PSE Method relies on studying the solutions of the following system.

$$\begin{cases} c_{13}x_{30} = a_0(0), \\ (k_{21} + c_{13}k_{31})x_{10} - c_{13}^2x_{30} = a_1(0), \end{cases} \quad (5)$$

According to Theorem 2, it is sufficient to find the solutions of (5). From the first equation, one gets  $c_{13} = a_0(0)/x_{30}$ . Then, if  $0 \in [\underline{x}_{10}, \bar{x}_{10}]$ , the model is not globally SM identifiable since the particular case  $x_{10} = 0$  induces the following equations  $a_k(0) = (-1)^k c_{13}^{k+1} x_{30}$  for all  $k \geq 0$ . Otherwise, if  $0 \notin [\underline{x}_{10}, \bar{x}_{10}]$ , the second equation gives:

$$k_{21} = \frac{a_1(0) - c_{13}k_{31}x_{10} + c_{13}^2x_{30}}{x_{10}}. \quad (6)$$

Denote by  $\gamma$  the right member of (6). Solutions of (5) are in  $P^* = [\underline{\gamma}, \bar{\gamma}] \times [a_0(0), \bar{a}_0(0)]/[\underline{x}_{30}, \bar{x}_{30}]$  and according to Theorem 2, the system (4) is globally SM identifiable for  $P^*$ .

Furthermore, the function  $\phi : (k_{21}, c_{13}) \mapsto c_{13}x_{30}, (k_{21} + c_{13}k_{31})x_{10} - c_{13}^2x_{30}$  is  $(P^*, \mathbb{R}^2)$ -injective. Thus, the system (4) is  $\mu$ -set membership identifiable for  $P^*$ .

Obviously, this method can be used for the construction of  $P^*$  as it can be seen easily in example 1 but a better estimate can be

<sup>2</sup> Recall that intervals are denoted  $[\underline{x}, \bar{x}] = \{x \in \mathbb{R}, |\underline{x} \leq x \leq \bar{x}\}$ .

obtained by using indirect methods and the whole measurement trajectory. However, it permits to know (in certain cases easily) if the model can be or not  $\mu$ -set- membership identifiable and if some points in the interval parameters have to be excluded.

### 4.3 Differential Algebra based Method (DA Method)

In this subsection, the method proposed by Denis-Vidal et al. [2001] based on differential algebra and taking into account the initial conditions is adapted for studying the ( $\mu$ -)SM identifiability.

This method consists in eliminating unobservable state variables in choosing the appropriate elimination order  $\{p\} < \{y, u\} < \{x\}$ . Then, the differential algebra approach Kolchin [1973] allows one to obtain relations between outputs, inputs and parameters. These relations can be expressed as:

$$R_i(y, u, p) = m_0(y) + \sum_{k=1}^{n_i} \theta_k^i(p) m_k(y, u), \quad i = 1, \dots, m, \quad (7)$$

where  $(\theta_k^i)_{1 \leq k \leq n_i}$  are rational in  $p$ ,  $\theta_u^i \neq \theta_v^i$  ( $u \neq v$ ),  $(m_k)_{1 \leq k \leq n_i}$  are differential polynomials with respect to  $y, u$  and  $\theta_0 \neq 0$ .

The size of the system is the number of observations. For simplicity, we suppose that  $i = 1$ , that is there is one output and  $n_1 = n$ .

The following theorem permits to obtain necessary and sufficient conditions for having global SM identifiability or  $\mu$ -SM identifiability.

Consider  $l$  the higher order derivative of  $y$  in (7).

**Theorem 4.** Assume that the functional determinant  $\Delta R(y) = \det(m_k(y, u), k = 1, \dots, n)$  is not in the ideal  $\mathcal{I}_p^0$  obtained after eliminating state variables.

Consider  $P^*$  a subset of  $\mathcal{U}_P$  for which the function  $\phi : p = (p_1, \dots, p_p) \mapsto (\theta_1(p), \dots, \theta_n(p), y(t_0^+, p), \dots, y^{(l-1)}(t_0^+, p))$  verifies:

$$\forall p^* \in P^*, \forall \bar{p} \notin P^*, \phi(p^*) \neq \phi(\bar{p}). \quad (8)$$

Then the model  $\Gamma_1^P$  is globally SM identifiable for  $P^*$ .

If the model  $\Gamma_1^P$  is globally SM identifiable for  $P^*$  and  $\phi$  is  $(P^*, \mathbb{R}^P)$ -injective then the model is  $\mu$ -SM identifiable for  $P^*$ .

In the two cases, if the coefficient of  $y^{(l)}$  in (7) is not equal to 0 at  $t_0$ , then the reciprocal is valid.

**Proof – Sufficiency** Let  $P^*$  verify the hypothesis of the theorem. Suppose there exists an input  $u^*$  such that  $Y(P^*, u^*) \neq \emptyset$  and  $y^* \in Y(P^*, u^*) \cap Y(\bar{P}, u^*)$  for a cartesian product of intervals  $\bar{P} \in \mathcal{U}_P$ . Thus, there exists  $p^* \in P^*, \bar{p} \in \bar{P}$  such that  $y^*(\cdot) = y(\cdot, p^*) = y(\cdot, \bar{p})$  and  $R(y^*, u^*, p^*) = R(y^*, u^*, \bar{p})$ .

Denote  $Q(y^*, u^*) = R(y^*, u^*, p^*) - R(y^*, u^*, \bar{p})$ . Since  $\det(Q)(y^*, u^*) = \det(m_k(y^*, u^*), k = 0, \dots, n) = \Delta(R)(y^*, u^*)$  is not equal to zero,  $\theta_k(p^*) = \theta_k(\bar{p})$  for  $k = 1, \dots, n$ . Besides, we have  $y(\cdot, p^*) = y(\cdot, \bar{p})$  in particular  $y^{(k)}(t_0, p^*) = y^{(k)}(t_0, \bar{p})$  for  $0 \leq k \leq l-1$ . Since the function  $\phi$  is supposed to verify the condition (8), one gets  $\bar{p} \in P^*$  and  $P^* \cap \bar{P} \neq \emptyset$ .

If  $\phi$  is  $(P^*, \mathbb{R}^P)$ -injective,  $P^*$  can be as small as possible and we always have  $p^* = \bar{p}$  that is  $P^* \cap \bar{P} \neq \emptyset$ .

**Necessity** Let's prove the contrapositive. Suppose there exists  $\bar{P}$ , such that  $P^* \cap \bar{P} = \emptyset$  and  $\phi(p^*) = \phi(\bar{p})$  for a certain  $p^* \in P^*$  and a  $\bar{p} \in \bar{P}$ . Since the coefficient of  $y^{(l)}$  in (7) is not

equal to 0 at  $t_0$  and the differential polynomials  $(m_k)_{k=1, \dots, n}$  have a degree 1 in  $y^{(l)}$  (Denis-Vidal et al. [2001]), any time derivative  $y^{(r)}(t_0^+, p^*)$ ,  $r \geq l$  can be rewritten in function of  $y^{(l-1)}(t_0^+, p^*), \dots, y(t_0^+, p^*), \theta_1(p^*), \theta_n(p^*)$ . According to the hypothesis on  $\phi$ , the  $(l-1)$  first coefficients of  $y(t, p^*)$  in the Taylor expansion are the same as those of  $y(t, \bar{p})$ , thus  $y^* := y(t, p^*) = y(t, \bar{p})$  and  $y^* \in Y(P^*, u) \cap Y(\bar{P}, u)$ . Thus, the model is not globally-SM identifiable for  $P^*$ .  $\square$

**Example 2:** Consider the uncertain model:

$$\begin{cases} \dot{x}_1 = p_1 x_1^2 + \sin(p_2) x_1 x_2, & x_1(0) = 1 \\ \dot{x}_2 = p_3 x_1^2 + x_1 x_2, & x_2(0) = x_{20} \\ y = x_1. \end{cases} \quad (9)$$

where  $(p_1, p_2, p_3) \in \mathcal{U}_P = \mathbb{R} \times [0, 2\pi[ \times \mathbb{R}^+$  are the unknown parameters. Let  $p_4 = \sin(p_2)$ . In using the Rosenfeld-Groebner algorithm in Maple, the three following cases are given: the impossible one  $y = 0$  since  $y(0) = 1$ , the particular case  $p_4 = 0$  (thus  $p_2 = 0, \pi$ ) and the general characteristic presentation:

$$\mathcal{C} = \{y^2 - y\dot{y} + \dot{y}y^2 + p_1(\dot{y}y^2 - y^4) + p_4 p_3 y^4\}.$$

The functional determinant of  $\{y\dot{y}^2 - y^4, y^4\}$  is equal to  $2y^5\dot{y}^2 - y^6\ddot{y}$ . With the function *belong\_to* of the package Maple, we verify that the functional determinant is not in  $\mathcal{I}_p^0$ .

Thus, we have to study the following function  $\phi : (p_1, p_2, p_3) \rightarrow (p_1, \sin(p_2)p_3, p_1 + \sin(p_2)b)$ .

The model is globally SM identifiable for  $P_1^* = \mathbb{R} \times ]0, \pi[ \times \mathbb{R}^+$  and  $P_2^* = \mathbb{R} \times ]\pi, 2\pi[ \times \mathbb{R}^+$ . Indeed, it is sufficient to remark that  $\forall p_2^* \in ]0, \pi[, \forall \bar{p}_2 \in ]\pi, 2\pi[, \sin(p_2^*) > 0$  and  $\sin(\bar{p}_2) < 0$ . However, the model is clearly not  $\mu$ -SM identifiable for  $P_1^*$  and  $P_2^*$  since the function  $\sin$  is not injective on these two subsets.

## 5. PARAMETER ESTIMATION

In this section, a numerical method deduced from section 4.3 is proposed to estimate the unknown constant parameters of a non linear system like (1). We consider the case  $i = 1$ , that is there is only one output variable.

The output is supposed to be disturbed by a bounded additive noise  $\eta$ ,  $\eta(t) \in [\eta(t)]$  and the parameter vector  $p$  belongs to  $P$  where  $P$  is an interval vector. The polynomial (7) can be used to estimate the interval vector  $P$ . Consider  $\Theta_k(P)$  the associated expression of  $\theta_k(p)$  defined in the polynom (7), where  $p$  is substituted by  $P$ .  $\Theta_k(P)$  is a connected set for all connected  $P$  since it involves sum, difference and product of connected sets.

Suppose that the observations are done at discrete times  $t_j$ ,  $0 \leq j \leq M$  and they are noted  $y_j = y(t_j)$ . Then, the following system whose interval vector  $(\Theta_k(P))_{1 \leq k \leq n}$  is unknown can be deduced:

$$\forall j = 0, \dots, M, 0 \in m_0(y_j, u_j) + \sum_{k=1}^n \Theta_k(P) m_k(y_j, u_j). \quad (10)$$

Notice that (10) is linear with respect to  $\{\Theta_1(P), \dots, \Theta_n(P)\}$ . Parameter estimation consists in solving the previous system which comes back to solving  $0 \in [A][x] - [b]$  or  $[A][x] = [b]$  where  $[A]_j = ([m_1(y_j, u_j)], \dots, [m_n(y_j, u_j)])$  is the  $j^{\text{th}}$  line of  $[A]$  and  $[b]_j = [-m_0(y_j, u_j)]$  is the  $j^{\text{th}}$  line of  $[b]$ .

**Example 3:** The following example taken from (Verdière et al. [2005]) is considered. It allows one to explore the capacity

of the macrophage mannose receptor to endocytose soluble macromolecule and to quantify the different aspects of such a process. The model is the following:

$$\begin{cases} \dot{x}_1 = \alpha_1(x_2 - x_1) - \frac{V_m x_1}{1 + x_1}, \\ \dot{x}_2 = \alpha_2(x_1 - x_2), \\ x_1(0) \in [0.62, 0.63], x_2(0) = 0, \\ y = x_1, \end{cases} \quad (11)$$

where  $x_1$  (resp.  $x_2$ ) is the enzyme concentration outside (resp. inside) the macrophage and  $p = (\alpha_1, V_m, \alpha_2)$  are the unknown parameters which have to be identified. The parameter  $\alpha_1$  is the rate constant of the transfer from Compartment 1 (or the central compartment), practically plasma, to Compartment 2 (or the peripheral compartment), which represents in the model the part of the extravascular extracellular fluid accessible. Furthermore,  $\alpha_2$  is the rate constant of the transfer from Compartment 2 to Compartment 1.

The study has been conducted in simulation in Matlab by using Intlab. The simulated outputs are disturbed by a truncated gaussian noise  $\eta$  such that  $\eta(t) \in [-0.001, 0.001]$ . Thus,  $y(t) = \bar{y}(t) + \eta(t)$  where  $\bar{y}$  is the exact output corresponding to the exact value of parameters:  $\alpha_1 = 0.011$ ,  $\alpha_2 = 0.02$  and  $V_m = 0.1$ . The observations are supposed to be done at discrete times  $(t_j)_{j=1, \dots, N}$  on the interval  $[0, 117]$  with a sampling period equal to  $\frac{1}{2}$ . The polynomial  $R(y, u)$  is given by:

$$R(y, u) = \ddot{y}(1+y)^2 + \gamma_1 \dot{y}(1+y)^2 + \gamma_2 y(1+y) + \gamma_3 \dot{y},$$

with  $\gamma_1 = \alpha_1 + \alpha_2$ ,  $\gamma_2 = \alpha_2 V_m$  and  $\gamma_3 = V_m$ .

If we denote  $y_p(t_j)$  (resp.  $y_{pp}(t_j)$ ) the estimate of  $\dot{y}(t_j)$  (resp.  $\ddot{y}(t_j)$ ). These estimates are obtained by finite differences and the obtained system which has to be solved is  $[A][\gamma] = [b]$  where  $[A]_j = ([y_p(t_j)(1+y(t_j))^2], [y(t_j)(1+y(t_j))], [y_p(t_j)])$  and  $[b]_j = [-y_{pp}(t_j)(1+y(t_j))^2]$ .

Solving this system can be casted into the set inversion framework for which we used the SIVIA algorithm. To use SIVIA, it is necessary to give initial intervals for  $\gamma_1$ ,  $\gamma_2$  and  $\gamma_3$ . The problem solved here is to find  $[\gamma]$  such that  $0 \in [A][\gamma] - [b]$ . By using initial intervals given by  $[\gamma_1] = [0, 0.04]$ ,  $[\gamma_2] = [0, 0.003]$ ,  $[\gamma_3] = [0, 0.2]$  and the bisection precision  $\varepsilon = 0.001$ , we obtain in 14.18 seconds:  $[\alpha_1] = [0, 0.0401]$ ,  $[\alpha_2] = [0, 0.0437]$ ,  $[V_m] = [0.06875, 0.13203]$ . All these intervals contain the normal values.

Then, by using  $[\gamma_1] = [0, 0.04]$ ,  $[\gamma_2] = [0, 0.003]$ ,  $[\gamma_3] = [0, 0.2]$  and the bisection precision  $\varepsilon = 0.0001$ , we obtain in 177.55 seconds:  $[\alpha_1] = [0, 0.0329]$ ,  $[\alpha_2] = [0.0071, 0.0317]$  and  $[V_m] = [0.094824, 0.10527]$ . All these intervals contain the normal values.

## 6. CONCLUSION

This paper summarizes the quite scarce works for analysing the identifiability of SM models and presents the definitions of SM identifiability and  $\mu$ -SM identifiability. Checking these properties for the general case of non linear systems is the main focus of the paper. Interestingly, a parameter estimation method is derived from one of the identifiability checking methods. By building the parameter estimation scheme on the analysis of identifiability, we can guarantee that the solution set reduces to one connected set. Future work will consider to apply the parameter estimation method in various application domains. Fault detection and identification will be our preferred line of work and the prognosis problem will also be considered.

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